UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/646,763 | 10/24/2000 | Michel Lanquetin | GEI-078 | 8985 |

7590 12/17/2002

Bierman Muserlian and Lucas
600 Third Avenue
New York, NY 10016

| EXAMINER |
|---|
| HUI, SAN MING R |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | 17 |

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/646,763 | Applicant(s) LANQUETIN ET AL. | |
|---|---|---|---|
| | Examiner San-ming Hui | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3 and 5-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 23, 2002 has been entered.

The amendments of claims 11 and 14 filed April 1, 2002 have been entered.

Claims 1, 3, and 5-18 are pending.

### *Claim Objections*

Claim 11 is objected to because of the following informalities: the use of parenthesis in claim 11, line 6: "(Ethocel)", is considered improper. Appropriate correction is required.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-8, 11, 12, 14-15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saunal et al. (WO96/30000, English equivalent: USPN

6,010,716 is also provided), reference of record, and Maillo et al. (EP 0 785 211 A1) in view of Winters et al. (WO95/30409), reference of record.

Saunal et al. teaches a transdermal topical formulation employing a solvent, absorption promoting agent, an active, comprising the steroid, nomegestrol, and a film-forming agent. Saunal et al. teaches the composition may contain 0.1 to 20.0% of nomegestrol (See col. 5, line 28). Saunal et al. also teaches the solvent or solubilizing agent may be ethanol or isopropanol(See col. 7, line 13). Sanual et al. also teaches that the weight ratio of the ethanol may be 44% to 84.9% (See particularly col. 7, line 41-46). The film-forming agent is a cellulose derivative, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose succinate acetate, and ethylcellulose. (See col.3, line 58-63). The film-forming agent of Saunal et al. can also be PVP VA, a known polyvinylpyrrolidone derivative (See col. 3, line 67).

Maillo et al. teaches a gel formulation for topical use containing progesterone compounds encompassed nomegesterol, with 20 to 40% of ethyl alcohol, 1 to 4% of polyethylene glycol, and water (See page 9, line 41; also page 18, line 25-40, Example 22).

The references do not expressly teach the amount of nomegestrol as 0.05 to 1% in the composition. The references do not expressly teach film-forming agent as methacrylates, and cellulose. The references do not expressly teach a plasticizing agent such as Labrasol®, a preferred $C_8/C_{10}$ polyoxyethylene glycosyl glyceride herein. The references do not expressly teach the ratio of water, ethanol, propylene glycol, and Labrasol in preferred the solvent system herein. The references do not expressly teach

a method of employing the topical nomegestrol composition to treat progesterone deficiency in a host.

Winters et al. teaches a topical formulation of the steroid, 19-nor progesterone for systemic delivery of active. The formulation has a solvent which may include alcohols (See page 4, line 1-2), film-forming agent such as methacrylates, and cellulose (See page 4, line 8-11), a plasticizing agent such as Labrasol (See page. 4, line 18), and a penetration enhancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the amount of nomegestrol herein and a film-forming agent such as methacrylates and cellulose, and Labrasol into the nomegestrol topical composition of Saunal et al. It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the ratio of water, ethanol, propylene glycol, and Labrasol in preferred the solvent system herein.

The employment of nomegestrol as an active agent in a topical pharmaceutical composition with carrier materials herein is motivated because these carrier materials, such as methacrylates and cellulose, and Labrasol, are known pharmaceutical excipients, known to be useful in substantially similar topical pharmaceutical compositions comprising the same and similar active ingredients. The incorporation of known carrier materials into a pharmaceutical composition containing a known active is considered within the skill of the artisan.

The optimization of result effect parameters (e.g., amounts of ingredients) is obvious as being within the skill of the artisan, absent evidence to the contrary.

Amounts of composition ingredients employed herein are substantially similar to the prior art.

The instant composition containing nomegestrol would be reasonably expected to be similarly useful to raise progesterone levels in a host, regardless of their status as being menopausal or premenopausal, and treating progesterone deficiency thereby.

Claims 9-10, 13, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saunal et al. and Maillo et al. in view of Winters et al. as applied to claims 1, 3, 5-8, 11, 12, 14-15, and 18 above, and further in view of Merck Index (Budavari et al., editor, Merck Index, 12th ed., 1996: page889-890, Compound 5232), Eibl et al. (USPN 5,290,769), and Remington's Pharmaceutical Sciences (Gennaro et al., Remington's Pharmaceutical Sciences, 18th ed., 1990: page 1305), reference of record.

The combination of Saunal et al., Maillo et al., and Winters et al. does not expressly teach the employment of isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer in the topical nomegestrol composition. The combination of Saunal et al., Maillo et al., and Winters et al. does not expressly teach the ratio of propylene glycol and isopropylidene glycerol.

The Merck Index teaches that isopropylidene glycerol may be used as a solubilizing or plasticizing agent in pharmaceutical compositions (See page 889-890, Compound 5232).

Eibl et al. teaches the use of copolymer of methacrylic acid and ethyl acrylate as pharmaceutical auxiliary agents in topical formulation (See col 5, line 66 and col. 6, line 19-20).

Remington's Pharmaceutical Sciences teaches that carbomer is useful as a gelling and emulsifying agent in pharmaceutical compositions (See page 1305, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer into the topical nomegestrol composition.

One of ordinary skill in the art would have been motivated to incorporate isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer into the topical nomegestrol composition since isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer are known as agents for topical pharmaceutical excipients. Incorporating any known excipients, including isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer, into the topical nomegestrol composition would be considered as being within the purview of skilled artisan. Furthermore, the optimization of the amount ratio between propylene glycol and isopropylidene glycerol would be obvious as considered being within the purview of skilled artisan.

***Response to Arguments***

Applicant's arguments filed April 1, 2002 regarding the difference of transdermal and topical composition have been addressed in the Advisory action mailed April 23,

2002. Please note further that, in response to applicant's remarks on Saunal et al. teaching a composition for transdermal delivery, the instant composition is also a composition for transdermal delivery of the active because the instant composition is also intended for systemic delivery of progesterone (See claim 1). Saunal et al. clearly teaches a nomegestrol containing composition comprising the herein claimed film-forming agents and a penetration enhancer.

Applicant's arguments filed April 1, 2002 regarding the solvent systems have been considered, but are not found persuasive. All the solvents employed herein are commonly used and well-known solvents used in the pharmaceutical topical composition. Mixing and/or combining these herein claimed solvents, which are commonly known in formulating topical composition, for formulating topical composition would be obvious, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
December 9, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

12/11/02